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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,718	01/04/2002	Ralph Evan McGinnis	2DLSM&R12/01	7724

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EXAMINER	
WHALEY, PABLO S	
ART UNIT	PAPER NUMBER
1631	
MAIL DATE	DELIVERY MODE
10/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/037,718	MCGINNIS ET AL.	
	Examiner	Art Unit	
	PABLO WHALEY	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2009 and 24 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *91-93,104,105,108,109 and 167-235* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *91-93,104,105,108,109 and 167-235* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/11/2009* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 91-93, 104, 105, 108, 109, 167-235 are currently pending and under consideration.

Claims 1-90, 94-103, 106, 107, and 110-166 are cancelled.

Specification

The specification repeats the priority claim on multiple pages (see pages 1, 9, and 49). These priority claims all appear to be the same. Therefore, applicant should delete the duplicate priority claim paragraphs on pages 9 and 49 if they merely repeat the priority claim on page 1. If they are different, applicant should move them to the first paragraph of the specification.

Information Disclosure Statement

The information disclosure statements filed 06/11/2009 have been considered in full.

Priority

Applicant's arguments filed 03/10/2009 regarding priority have been fully considered but are not persuasive. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). Amended claim 91 now requires the limitations "wherein the CL-F region is a segment-subrange,...whereby the length of the segment is

greater than or equal to about 47 million base pairs, wherein the subrange of the segment-subrange includes the least common allele frequency 0.1, whereby there are at least about 24 covering markers with least common allele frequencies less than or equal to 0.3 that are distributed within the segment with a density of at least about 1 marker every two million base pairs. The disclosures of the prior-filed applications 09/947,768 and PCT/US99/04376 both fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. In particular, while the disclosures of 09/947,768 and PCT/US99/04376 describe linkage disequilibrium studies and generally state "it is possible for the chromosomal location distance component of 8 to be as large as about 10 to 12 cM, about 10 to 12 million bp, or the equivalent thereof for homogeneous human populations" this fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for claim 91 of this application as amended.

Withdrawn Rejections

The rejection of claims 91-139 under 35 U.S.C. 103(a) as being unpatentable over Cohen (1997), in view of Kruglyak and Cohen (1999) is withdrawn in view of applicant's amendment filed 04/24/2009.

The rejection of claims 91-139 under 35 U.S.C. 103(a) as being unpatentable over McGinnis in view of Cohen (1999) is withdrawn in view of applicant's amendment filed 04/24/2009.

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

This rejection is necessitated by amendment.

Claims 91-93, 104, 105, 108, 109, 167-235 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. In considering the factors for the instant claims:

a) Quantity of experimentation: The utility of the claimed invention is well-established, as set forth in instant claim 91 drawn to oligonucleotide compositions for obtaining genotype data or sample allele frequency data. An assert utility is also provided in the specification [p.48, last ¶]. In order to practice the claimed invention one of skill in the art must determine a set of oligonucleotides that are complementary to a set of covering markers specifically chosen so that a CL-F region is N-covered to within specific [x,y] two-dimensional distances according to functional limitations set forth in claim 91. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The amount of direction or guidance presented: The claimed invention is drawn to a composition, more specifically a set of oligonucleotides that are complementary to a set of covering markers specifically chosen according to the functional limitations set forth in claim 91. The specifically generally discusses conventional techniques for choosing a set of markers for scanning chromosomal regions [p.4, 5]. The specification generally describes principles and concepts for using a set of oligonucleotides, technology for genotyping of individuals, and theoretical linkage studies and power

analysis for bi-allelic covering markers [See at least p.21, 22, 32, 35, 36, 37, 39]. The specification does not provide specific guidance such that one of skill in the art would know how to obtain a set oligonucleotides which are complementary to a set of covering markers specifically chosen to meet specific functional limitations described in the claims, which include least common allele frequency and two-dimensional distance calculations [See for example claims 91, 93, 104, 108, 109, 171, and 220]. For example, the specification does not provide specific guidance for producing a set of oligonucleotides that are complementary to a set of covering markers chosen so that a CL-F region is N-covered to within specific [x,y] distances, as in claim 91. It is noted that these functional limitations are confusing because the do not explicitly limit the structure of the claimed oligonucleotides, per se, but instead further limit the method by which the complementary group of covering markers are obtained. Additionally, the specification does not provide any guidance such that one of skill in the art would know how to obtain a set oligonucleotide compositions which are complementary to a set of covering markers that systematically covers a CL-F region that is N-covered to within [x,y], wherein x is less than or equal to 1 million base pairs and y is less than or equal to 0.2, and wherein N is less than maximal, and whereby the number and distribution of known markers in the neighborhood of the CL-F region make it possible for N to be a greater value, or whereby the CL-F region is a segment-subrange that is greater than or equal to the length of the human chromosome 21, as in claim 91. Additionally, regarding the asserted utility described above, the specification does not provide any guidance on obtaining the claimed compositions and using them for detecting specific genetic disorders in a defined population.

c) The presence or absence of working examples: The specification provides working examples for genotyping individuals using bi-allelic markers to test for linkage and association [p.35, 36, 44, 48]. The specification provides an example showing the importance of marker heterozygosity [p.42]. The specification does not provide working examples for obtaining a set oligonucleotide compositions that are complementary to a set of covering markers specifically chosen to meet the specific functional limitations

described in the claims, as discussed above.

d) The nature of the invention: The nature of the invention, oligonucleotides for use on obtaining genotype data or sample allele frequency data and linkage analysis, is complex.

e) The state of the prior art: One of skill in the art, after reading the specification, would not know how to produce a set of oligonucleotides that are complementary to a set of covering markers chosen so that a CL-F region is N-covered to within specific [x,y] distances and wherein the CL-F region includes specific least common allele frequencies, according to the claims, or that such compositions would allow for prediction of disease with increased power (as asserted in applicant's remarks filed 03/10/2009, page 28). The specification does not provide experimental evidence that oligonucleotides, being complementary to covering markers according to the limitations of claim 91, have been produced. Neither the prior art nor post-filing art shows oligonucleotides obtain according to the criteria set forth in the claims.

Cohen (1997) teaches methods for obtaining oligonucleotides to detect the presence of bi-allelic sites that are in linkage disequilibrium with genes used in determining the risk of prostate cancer [Col. 6, lines 5-25, Col. 16, Example 2]. Methods of candidate gene identification are described. However, mutations must be identified and oligonucleotide primers must be designed in order to amplify the sequences of every predicted functional region. Sequence variations must be known by screening of specific populations, which inherently have variability [See Col. 12, 13]. Cohen (1997) does not teach producing oligonucleotides that are complementary to covering markers chosen according the claimed functional limitations of claim 91. Cohen (1997) does not teach mapping chromosomes as a function of least common allele frequency and chromosomal position.

McGinnis teaches two-dimensional linkage analysis techniques and oligonucleotides complementary to markers within specific CL-F distances in a CL-F region of CL-F maps [p.9, p.14-16, p.31, p.35, Example 1S, p.36, and Ref. Claims 51-88]. McGinnis does not teach oligonucleotides that

are complementary to a set of covering markers that systematically covers a CL-F region that is N-covered to within [x,y], wherein x is less than or equal to 1 million base pairs and y is less than or equal to 0.2, and wherein N is less than maximal, and whereby the number and distribution of known markers in the neighborhood of the CL-F region make it possible for N to be a greater value, or whereby the CL-F region is a segment-subrange that is greater than or equal to the length of the human chromosome 21, as in claim 91.

Delvin teaches linkage analysis methods for measuring marker performance and mapping genes to regions of chromosomes based on disequilibrium and chromosomal location [See Abstract, Table 3, Fig. 1]. Delvin does not teach producing oligonucleotides that are complementary to covering markers chosen according the claimed functional limitations of claim 91, wherein a CL-F region is N-covered to within a specific [x,y] distance for example. Delvin does not teach mapping chromosomes as a function of least common allele frequency and chromosomal position.

f) The relative skill of those in the art: The skill of those in the art of genotyping and linkage analysis is high.

g) The predictability of the art: The predictability of obtaining oligonucleotides complementary to markers chosen according to claim 91 for use in obtaining genotype and allele frequency data is unknown in the prior art and is not described in the instant specification.

h) The breadth of the claims: The claims are broad in that they are drawn to oligonucleotides, being complementary to markers chosen so that a CL-F region is covered to within a specific [x,y] distance, who relationship to the claimed functional limitations recited in the claims is not established, and whose relationship to the use of these oligonucleotides in obtaining genotype and sample allele frequency data is not established. The skilled practitioner would first turn to the instant specification for guidance in using the claimed invention. However, the specification lacks any evidence that the claimed oligonucleotides, which are complementary to covering markers selected according to claim 91, are

capable of or related to identifying genes associated with a specific disease. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss oligonucleotide compositions which are complementary to a specific set of covering markers chosen to systematically cover a CL-F region according to specific distances, allele frequencies, and chromosome base pair lengths, as in claim 91. In fact, prior art shows that oligonucleotide primers must be designed in order to amplify the sequences of every predicted functional region, and therefore functional regions related to specific diseases and sequence variations in specific populations must be known [Cohen, See Col. 12, 13]. Finally, said practitioner would turn to trial and error experimentation to determine sets of oligonucleotides being complementary to specific sets of covering markers chosen based on specific distance, allele frequency, and chromosomal length limitations, according to claim 91, in various populations or species of creatures. Such amounts to undue experimentation.

Written Description

Claims 91-93, 104, 105, 108, 109, 167-235 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims, as currently written, are drawn to a set of oligonucleotides, being complementary to a set of covering markers chosen so that a CL-F region is N-covered to within specific [x,y] two-dimensional distances and wherein the CL-F region that is N-covered to within [x,y], wherein x is less than or equal to 1 million base pairs and y is less than or equal to 0.2, and wherein N is less than maximal, and whereby the number and distribution of known markers in the neighborhood of the CL-F region make it possible for N to be a greater value, the covering markers and CL-F region being for a species of creatures, and whereby the CL-F region is a segment-subrange that is greater than or equal to the length of the human chromosome 21, as in claim 91. The specifically generally discusses conventional

techniques for choosing a set of markers for scanning chromosomal regions [p.4, 5]. The specification generally describes principles and concepts for using a set of oligonucleotides, technology for genotyping of individuals, and theoretical linkage studies and power analysis for bi-allelic covering markers [See at least p.21, 22, 32, 35, 36, 37, 39]. However, the specification does not provide any disclosure of oligonucleotide compositions (e.g. specific SEQ ID numbers) obtained according to limitations set forth in the claims (See claim 91). Therefore one of ordinary skill in the art would have reasonable doubt that the applicant was actually in possession of such oligonucleotide compositions obtained in the way the instant claims describe at the time the application was filed.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 91-93, 104, 105, 108, 109, 167-235 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims that depend directly or indirectly from claim 91 are also rejected due to said dependence.

This rejection is necessitated by amendment.

Claim 91 recites "N is an integer greater than or equal to 1, wherein N is less than maximal, whereby the number and distribution of known markers in the CL-F region make is possible for N to be a greater value, as in claim 91. The terms "maximal" and "greater value" implies that N is selected by some existing criteria. However, the specification does not provide a standard or criteria for optimally selecting N such that one of ordinary skill in the art would know the metes and bounds of maximal and greater value, as claimed. Clarification is requested.

Response to Arguments

Applicant's arguments filed 03/10/2009 which assert that the equation on page 40 of the instant application, Table 2 on page 41 of the instant application and an unpublished manuscript constitute evidence of unexpected results have been fully considered. In response, Equation 2 represents the size of a signal for modeling data. While this equation may be useful for comparing disease models and may constitute a novel limitation if it were recited in the claim, merely pointing to an equation in the specification does not constitute an unexpected result. Regarding Table 2, the specification states that Table 2 illustrates how signal strength increases as marker and allelic frequencies become similar in magnitude [p.40]. Simply put, the table merely compares data for different modeled parameters. There is no evidence provided that explicitly compares applicant's power studies using bi-allelic markers with lower minor allele frequencies with those of the closest prior art. Therefore applicant's assertion of unexpected results constitutes mere argument.

Applicant's arguments [p.30-35] that conventional art shows highest heterogenosity gives the highest power (m=0.5), whereas the instant invention shows the highest heterogenosity gives the lowest power, it is noted that the instant claims are directed to a composition for use in obtaining genotype data or sample allele frequency. The instant claims do not recite any limitations drawn to determining the highest heterogenosity or lowest power.

Applicant's additional arguments are moot in view of the new grounds of rejections.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing

date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley

Patent Examiner

Art Unit 1631

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